

**X-RAY INVESTIGATION ON ACRIDINE DERIVATIVES. PART I.  
CRYSTAL AND MOLECULAR STRUCTURE OF  
1-NITRO-9(3-DIMETHYLAMINOPROPYLAMINO)-ACRIDINE  
HYDROIODIDE \***

by Zbigniew DAUTER, Maria BOGUCKA-LEDÓCHOWSKA, Andrzej  
HEMPPEL, Andrzej LEDÓCHOWSKI, and Zofia KOSTURKIEWICZ

*Department of Pharmaceutical Technology and Biochemistry,*

*Polytechnical University, 80952 Gdańsk*

*Department of Crystallography, A. Mickiewicz University, 60780 Poznań*

W wyniku rentgenowskiej analizy strukturalnej związku tytułowego określono strukturę krystaliczną i cząsteczkową oraz przeprowadzono szczegółową dyskusję.

Методом рентгеноструктурного анализа расшифрована и детально продискутирована кристаллическая и молекулярная структура заглавного соединения.

Crystal and molecular structure of the title compound has been determined by use of X-ray crystallographic methods and is discussed in detail.

$N^9$ -Derivatives of 1-nitro-9-aminoacridine<sup>1)</sup> exhibit a potent anti-neoplastic activity *in vivo* and *in vitro* in a number of biological tests<sup>1,2)</sup>. One of this derivatives is 1-nitro-9(3-dimethylaminopropylamino)-acridine dihydrochloride (designated as C-283) which has been registered in Poland as anti-neoplastic drug under the name Ledakrin, having previously undergone extensive pre-clinical and clinical investigations<sup>3)</sup>. It shows highly pronounced specificity not only in its biological activity but also in some chemical aspects, e.g. in hydrolysis<sup>4)</sup>, in polarographic<sup>5)</sup> investigations, etc. To elucidate the high specificity of the properties of this medicine, the crystal structure of the monoiodide form of this compound has been analyzed by X-ray methods. Results of the analysis are reported in this paper.

**EXPERIMENTAL AND CRYSTAL DATA**

Single crystals of 1-nitro-9(3-dimethylaminopropylamino)-acridine hydroiodide were grown from methanol in ethyl ether atmosphere in form of thin yellow needles elongated along the c axis. Preliminary precession photographs showed the crystals to be orthorhombic. The observed crystal density was obtained by flotation in aqueous potassium iodide.

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Crystal data:  $C_{18}H_{21}N_4O_2I$ .  $a = 24.53$  (2),  $b = 19.94$  (2),  $c = 7.83$  (1) Å; systematic absences  $0kl$ ,  $k = 2n+1$ ;  $h0l$ ,  $l = 2n+1$ ;  $hk0$ ,  $h = 2n+1$ , space group  $Pbca$ ;  $Z = 8$ ,  $M = 452.2$ ,  $D_o = 1.57$ ,  $D_c = 1.59$  g·cm $^{-3}$ ;  $F(000) = 1808$ ,  $\lambda$  (for CuK $\alpha$ ) = 1.5418 Å.

The dimensions of the crystal selected for analysis were  $0.2 \times 0.01 \times 0.4$  mm. Cell dimensions were calculated by least-squares refinement of 16 high-angle reflexions measured on a diffractometer. Intensity data collection was performed on a Hilger-Watts fully automatic four-circle diffractometer using graphite-monochromatized CuK $\alpha$  radiation. The  $c$  axis of the crystal coincided with the  $\varphi$  axis of a four-circle goniostat. Integrated intensity measurement were made by scanning the reflexions with the  $\Theta : 2\Theta$  scan technique at a rate of 1° per minute over a  $2\Theta$  range of 2°. The background was counted for 20 s at each of the scan limits. During the data collection process the intensity changes of the standard reflexion were recorded after every 50 measurements, showing crystal and instrumental stability; the maximum intensity variation observed was 1.3% of the mean value. Totally, 1663 independent reflexions with  $\sin \Theta / \lambda < 0.5$  were measured; 163 of these reflexions had  $I$  (net) intensity values less than  $3\sigma(I)$  where  $\sigma(I)$  is given by  $[N + k^2(N_{B1} + N_{B2})]^{1/2}$ . In this expression  $N$  is the total number of counts collected during scanning,  $N_{B1}$  and  $N_{B2}$  are the background measurements at either end of the scan range,  $k$  is the ratio  $T_{\text{scan}}/T_{\text{bkg}}$  of the total scan time to the total background scan time. The intensities were corrected for Lorentz and polarization effects. Because of the non-isometric shape of the crystal, semi-empirical absorption corrections were made. The variation in intensity of the axial reflexion (004) was measured during rotation of the crystal around the goniometer  $\varphi$  axis to obtain curve  $A$  of relative transmission against the azimuthal angle  $\varphi$  for the corresponding reciprocal lattice level. The curve is shown in Fig. 1.

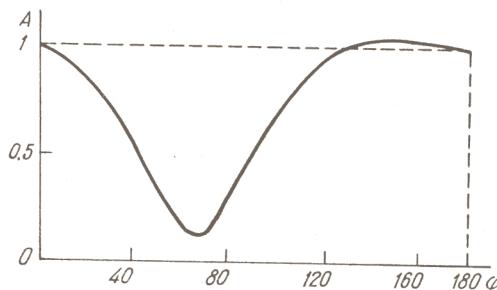


Fig. 1. Curve  $A$  relative transmission against the azimuthal angle  
Rys. 1. Zależność względnej transmitancji  $A$  od kąta azymutalnego

Reduction to structure amplitudes and absorption correction calculations were performed during data collection using the Hilger-Watts Software System. Observed and calculated structure factors are given in Table 1\*.

#### Structure determination and refinement

The first stage of the analysis aimed at locating the iodide ion in the asymmetric unit and was carried out both by heavy-atom and direct methods.

In order to use direct methods the observed 1500 reflexions were converted to values of normalized structure factors,  $|E|$ , by means of the formula<sup>6)</sup>

$$E_{hkl}^2 = \frac{F_{hkl}^2}{\varepsilon \sum_j f_j^2}$$

In the  $Pbca$  group  $\varepsilon$  is 4 for  $h00$ ,  $0k0$  and  $00l$  type reflexions,  $\varepsilon$  is 2 for  $0kl$ ,  $h0l$  and  $hk0$  type reflexions<sup>6,7)</sup>. The statistical distributions and the corresponding averages, of the normalized structure factors  $|E|$  are given in Table 2. The 286 highest  $|E|$  values

\* A list of structure factors (Table 1) may be obtained from the authors on request.

Table 2 — Tablica 2  
Distribution of normalized structure factors

Rozkład statystyczny znormalizowanych czynników struktury

	C—283.HI	Theoretical	
		I	I'
$\langle  E  \rangle$	0.827	0.798	0.886
$\langle E^2 \rangle$	1.000	1.000	1.000
$\langle  E ^2 - 1 \rangle$	0.951	0.968	0.736
% $E > 3.0$	0.20	0.30	0.01
2.5	1.53	1.24	0.19
2.0	4.40	4.55	1.83
1.8	6.93	7.19	3.92
1.6	10.19	10.96	7.73
1.4	15.79	16.15	14.09
1.2	22.32	23.01	23.69
1.0	29.98	31.73	36.79

with  $|E|$  greater than 1.30 were used to generate triple relationships. To specify the origin of the coordinate system in the  $Pbca$  space group the signs of three properly selected reflexions were arbitrarily assigned<sup>8)</sup>. These were:

$$\begin{array}{lll} 1 & 5 & 2 \quad (\text{uug}) \quad E = +3.780 & g - \text{gerade} \\ 9 & 2 & 3 \quad (\text{ugu}) \quad E = +3.246 & u - \text{ungerade} \\ 11 & 0 & 2 \quad (\text{ugg}) \quad E = -2.904. \end{array}$$

The phases of further 23 structure invariants were derived from the  $\Sigma_1$  formula with probabilities greater than 0.97<sup>8,9)</sup>. The application of the  $\Sigma_1$  formula is presented in Table 3.

Since we had 26 signs before beginning the procedure of symbolic addition, the signs for 282 out of the 286 highest  $|E|$  values could be determined on the basis of the  $\Sigma_2$  relationship<sup>6)</sup>. The sign-generating procedure went smoothly and no symbols were introduced. The  $E$  map based on 282 phased  $E$ 's revealed the position of the iodide ion. Its coordinates are shown in Table 4. The atomic scattering factors for C, N, O, H and I were taken from *International Tables for X-ray Crystallography*<sup>10)</sup>. The initial residual  $R_{\text{value}} = \sum [|F_o| - |F_c|]/\sum |F_o|$  calculated on the basis of the iodide ion coordinates at this stage was 0.35. A three-dimensional Fourier synthesis based on the phases of the iodide anion was computed. The positional parameters of 24 peaks were derived from the map. All peaks made good stereochemical sense, although some additional unreasonable maxima were still visible. However, a further map of electron density made on the basis of phases of all atoms of the molecule showed only the peaks attributed to real atoms. The  $R$  factor at this stage was 0.25.

Minimizing the quantity  $\Phi = \sum [|F_o| - |F_c|]^2$ , all fractional coordinates of 25 non-hydrogen atoms were refined by 4 cycles of block-diagonal least-squares with isotropic temperature factors. The  $R$  value was then reduced to 0.114. Further 2 cycles of anisotropic full-matrix least-squares approximation lowered the  $R$  value to 0.068. A three-dimensional difference Fourier synthesis performed at this stage revealed 15 peaks of nearly equal height. The hydrogen atom positions around the fused acridine ring system (eight atoms), at the methylene groups of the side chain (six atoms), and at the N(ω) nitrogen atom (one atom) were readily located. The remaining hydrogen atoms of the methyl groups were not found. This can be assumed to be due to thermal motions of the carbon atoms of the methyl groups ( $B_{\text{iso}}$  is equal 7). The hydrogen atom positions in the methyl groups cited above seems to undergo statistical distribution in the crystal structure as a result of free rotation around the N(22)—C(23) and N(22)—C(24) bonds. In the final stage of refinement, 2 cycles of full-matrix least-squares anisotropic calculations were performed for 25 non-hydrogen atoms and for the positional parameters of 15 hydrogen atoms.

Table 3 — Tablica 3

An application of  $\sum_1$  formulaZastosowanie wzoru  $\sum_1$ 

$2h$	$2k$	$2l$	$E_{2h,2k,2l}$	$P(+)$ , %
2	0	2	2.704	36.35*
2	4	0	-2.435	0.01
0	6	0	+2.022	99.96
2	10	0	-1.952	0.01
20	6	0	-1.934	0.01
4	4	0	1.850	95.69*
6	0	0	+1.824	97.64
16	6	0	-1.752	0.01
6	10	0	-1.749	0.01
4	0	0	+1.715	99.76
4	6	0	-1.691	1.42
16	10	0	+1.666	99.45
2	0	4	-1.598	0.01
2	6	0	+1.596	99.99
0	4	0	-1.581	0.26
0	10	4	+1.564	99.99
16	0	4	-1.449	0.07
0	10	0	-1.485	0.67
16	0	0	-1.443	0.13
20	10	0	+1.438	99.99
2	4	2	+2.137	99.92
2	2	4	+1.713	99.99
4	6	2	+1.586	99.95
2	10	4	+1.346	99.99
4	10	2	1.339	92.17*
4	4	4	+1.322	99.74

\* Probability less than 97% limit.

Table 4 — Tablica 4

Coordinates of iodide ion — Współrzędne jonu jodkowego

	$x/a$	$y/b$	$z/c$
Patterson map	0.028	0.155	0.153
$E$ -map	0.025	0.156	0.158
Refined	0.0276	0.1527	0.1545

The isotropic thermal parameters for hydrogens were not refined; all were established to have the same  $B_{iso}$  value 3.5. The  $R$  value finally obtained was 0.063. The refined fractional coordinates for all non-hydrogen atoms and corresponding anisotropic thermal parameters are presented in Table 5. The positional parameters of hydrogen atoms are given in Table 6.

T able 5 — Tablica 5

Final positional and thermal parameters of non-hydrogen atoms, standard deviations in parentheses (all quantities  $\times 10^4$ ). Temperature factors =  $\exp [-2\pi^2(h^2a^{*2}U_{11} + \dots + 2kb^*c^*U_{23})]$

Parametry pozycyjne i temperaturowe atomów niewodorowych; odchylenia standaryzowane w nawiasach (wszystkie wartości  $\times 10^4$ ). Czynniki temperaturowe =  $\exp [-2\pi^2(h^2a^{*2}U_{11} + \dots + 2kb^*c^*U_{23})]$

	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> <sub>11</sub>	<i>U</i> <sub>22</sub>	<i>U</i> <sub>33</sub>	<i>U</i> <sub>12</sub>	<i>U</i> <sub>13</sub>	<i>U</i> <sub>23</sub>
C (1)	2882 (6)	542 (8)	11194 (23)	290 (16)	417 (14)	431 (20)	-74 (12)	-43 (15)	40 (15)
C (2)	2654 (7)	-44 (8)	11801 (24)	445 (21)	512 (16)	410 (17)	-161 (22)	82 (13)	-46 (13)
C (3)	2090 (8)	-90 (9)	11756 (20)	756 (14)	389 (17)	419 (20)	-242 (12)	57 (18)	-59 (18)
C (4)	1771 (7)	427 (9)	11102 (25)	610 (19)	349 (15)	642 (19)	-30 (13)	182 (15)	59 (17)
C (5)	1545 (5)	2710 (9)	9546 (28)	308 (22)	411 (18)	887 (15)	188 (23)	95 (17)	116 (19)
C (6)	1751 (7)	3347 (9)	9406 (27)	311 (20)	469 (16)	790 (18)	161 (21)	89 (18)	118 (20)
C (7)	2286 (7)	3475 (9)	9426 (25)	653 (22)	387 (19)	610 (20)	226 (16)	118 (20)	111 (18)
C (8)	2649 (6)	2934 (8)	9517 (27)	418 (19)	345 (19)	649 (22)	113 (18)	-26 (21)	-47 (17)
C (9)	2826 (7)	1683 (7)	9681 (23)	427 (22)	244 (21)	398 (17)	-110 (16)	-4 (20)	-23 (16)
N (10)	1692 (5)	1517 (8)	9817 (20)	351 (20)	371 (17)	635 (18)	-20 (14)	45 (17)	13 (17)
C (11)	2584 (6)	1086 (7)	10483 (20)	229 (17)	254 (21)	504 (19)	-27 (17)	19 (16)	-23 (17)
C (12)	2008 (7)	1011 (8)	10495 (25)	451 (19)	214 (19)	533 (17)	-1 (15)	91 (17)	-24 (20)
C (13)	1883 (7)	2178 (9)	9694 (24)	384 (16)	449 (22)	470 (20)	-60 (17)	28 (19)	21 (17)
C (14)	2470 (6)	2268 (7)	9627 (22)	244 (18)	230 (19)	405 (25)	59 (20)	-3 (15)	-27 (16)
N (15)	3465 (6)	589 (8)	111440 (27)	555 (22)	469 (17)	826 (21)	9 (17)	-84 (18)	62 (19)
O (16)	3752 (6)	177 (7)	10659 (24)	582 (25)	679 (22)	1412 (22)	257 (19)	128 (19)	38 (21)
O (17)	3627 (5)	1021 (8)	12398 (21)	421 (18)	965 (23)	883 (20)	-217 (18)	-123 (19)	125 (22)
N (18)	3322 (5)	1609 (7)	9082 (17)	265 (17)	465 (21)	380 (19)	42 (17)	90 (18)	10 (20)
C (19)	3610 (6)	2129 (8)	8119 (22)	314 (19)	443 (14)	438 (22)	-30 (24)	108 (15)	99 (27)
C (20)	4068 (6)	1813 (9)	7232 (24)	247 (26)	685 (16)	437 (21)	128 (21)	-5 (17)	60 (22)
C (21)	4505 (7)	1600 (9)	8454 (29)	326 (23)	609 (19)	936 (28)	129 (20)	4 (20)	196 (19)
N (22)	4930 (5)	1164 (7)	7541 (21)	396 (19)	512 (16)	550 (22)	25 (17)	97 (22)	-86 (25)
C (23)	5461 (7)	1210 (13)	8497 (27)	360 (23)	1699 (28)	440 (23)	363 (20)	152 (26)	-130 (22)
C (24)	4760 (11)	425 (10)	7345 (41)	1262 (31)	488 (23)	1639 (29)	-224 (18)	486 (22)	53 (19)
I (25)	276 (1)	1526 (1)	11545 (2)	378 (10)	778 (8)	548 (5)	-41 (7)	-34 (8)	36 (5)

Table 6 — Tablica 6

Positional parameters of hydrogen atoms. Standard deviations in parentheses ( $\times 10^3$ )

Parametry pozycyjne atomów wodoru. Odchylenia standardowe w nawiasach ( $\times 10^3$ )

	<i>x</i>	<i>y</i>	<i>z</i>
H(26)	284 (6)	-45 (7)	1240 (22)
H(27)	198 (6)	-54 (7)	1228 (22)
H(28)	141 (6)	39 (8)	1142 (21)
H(29)	121 (5)	263 (8)	960 (21)
H(30)	152 (6)	368 (7)	947 (22)
H(31)	243 (7)	401 (8)	970 (20)
H(32)	308 (6)	302 (7)	888 (22)
H(33)	135 (6)	147 (8)	1024 (22)
H(34)	329 (6)	232 (9)	740 (23)
H(35)	364 (6)	240 (8)	879 (23)
H(36)	435 (7)	212 (7)	629 (22)
H(37)	381 (6)	151 (8)	627 (19)
H(38)	467 (5)	201 (9)	968 (20)
H(39)	441 (6)	113 (8)	964 (22)
H(40)	497 (6)	134 (8)	643 (20)

Table 7 — Tablica 7

Bond distances (Å) — Długości wiązań w Å

C(1)—C(2)	1.380 (23)	C(19)—C(20)	1.462 (22)
C(1)—C(11)	1.423 (21)	C(20)—C(21)	1.500 (25)
C(1)—N(15)	1.445 (22)	C(21)—N(22)	1.533 (23)
C(2)—C(3)	1.386 (25)	N(22)—C(23)	1.506 (23)
C(3)—C(4)	1.392 (28)	N(22)—C(24)	1.540 (25)
C(4)—C(12)	1.386 (24)	C(2)—H(26)	1.04 (11)
C(5)—C(6)	1.372 (29)	C(3)—H(27)	1.03 (11)
C(5)—C(13)	1.354 (24)	C(4)—H(28)	0.93 (10)
C(6)—C(7)	1.339 (24)	C(5)—H(29)	0.85 (9)
C(7)—C(8)	1.400 (24)	C(6)—H(30)	0.87 (11)
C(8)—C(14)	1.403 (21)	C(7)—H(31)	1.15 (12)
C(9)—C(11)	1.471 (21)	C(8)—H(32)	1.18 (15)
C(9)—C(14)	1.457 (21)	N(10)—H(33)	0.91 (11)
C(9)—N(18)	1.313 (20)	C(19)—H(34)	1.04 (9)
N(10)—C(12)	1.378 (22)	C(19)—H(35)	0.75 (13)
N(10)—C(13)	1.403 (23)	C(20)—H(36)	1.18 (15)
C(11)—C(12)	1.421 (21)	C(20)—H(37)	1.23 (16)
C(13)—C(14)	1.451 (22)	C(21)—H(38)	1.32 (21)
N(15)—O(16)	1.210 (23)	C(21)—H(39)	1.34 (19)
N(15)—O(17)	1.244 (24)	N(22)—H(40)	1.15 (17)
N(18)—C(19)	1.464 (20)		

Table 8 — Tablica 8  
Bond angles ( $^{\circ}$ ) — Kąty między wiązaniem

C(2)—C(1)—C(11)	125 (2)	C(4)—C(12)—C(11)	120 (2)
C(2)—C(1)—N(15)	114 (2)	N(10)—C(12)—C(11)	119 (1)
C(11)—C(1)—N(15)	121 (1)	C(5)—C(13)—N(10)	123 (2)
C(1)—C(2)—C(3)	117 (2)	C(5)—C(13)—C(14)	121 (2)
C(2)—C(3)—C(4)	121 (2)	N(10)—C(13)—C(14)	117 (2)
C(3)—C(4)—C(12)	121 (2)	C(8)—C(14)—C(9)	125 (1)
C(6)—C(5)—C(13)	120 (2)	C(8)—C(14)—C(13)	116 (1)
C(5)—C(6)—C(7)	122 (2)	C(9)—C(14)—C(13)	120 (1)
C(6)—C(7)—C(8)	119 (2)	C(1)—N(15)—O(16)	117 (2)
C(7)—C(8)—C(14)	122 (2)	C(1)—N(15)—O(17)	117 (2)
C(11)—C(9)—C(14)	115 (1)	O(16)—N(15)—O(17)	126 (2)
C(11)—C(9)—N(18)	116 (1)	C(9)—N(18)—C(19)	124 (1)
C(14)—C(9)—N(18)	129 (2)	N(18)—C(19)—C(20)	108 (1)
C(12)—N(10)—C(13)	122 (1)	C(19)—C(20)—C(21)	112 (2)
C(1)—C(11)—C(9)	125 (1)	C(20)—C(21)—N(22)	110 (2)
C(1)—C(11)—C(12)	115 (1)	C(21)—N(22)—C(23)	109 (1)
C(9)—C(11)—C(12)	119 (1)	C(21)—N(22)—C(24)	114 (2)
C(4)—C(12)—N(10)	121 (2)	C(23)—N(22)—C(24)	110 (2)

Table 9 — Tablica 9  
Dihedral angles ( $^{\circ}$ ) — Kąty dwuścienne

C(11)—C(1)—C(2)—C(3)	-2	N(18)—C(9)—C(11)—C(12)	-153
N(15)—C(1)—C(2)—C(3)	-176	C(11)—C(9)—C(14)—C(8)	156
C(2)—C(1)—C(11)—C(9)	-174	C(11)—C(9)—C(14)—C(13)	-24
C(2)—C(1)—C(11)—C(12)	3	N(18)—C(9)—C(14)—C(8)	-26
N(15)—C(1)—C(11)—C(9)	11	N(18)—C(9)—C(14)—C(13)	154
N(15)—C(1)—C(11)—C(12)	-173	C(11)—C(9)—N(18)—C(19)	175
C(2)—C(1)—N(15)—O(16)	65	C(14)—C(9)—N(18)—C(19)	-3
C(2)—C(1)—N(15)—O(17)	-115	C(13)—N(10)—C(12)—C(4)	160
C(11)—C(1)—N(15)—O(16)	-119	C(13)—N(10)—C(12)—C(11)	-161
C(11)—C(1)—N(15)—O(17)	62	C(12)—N(10)—C(13)—C(5)	-159
C(1)—C(2)—C(3)—C(4)	1	C(12)—N(10)—C(13)—C(14)	25
C(2)—C(3)—C(4)—C(12)	-1	C(1)—C(11)—C(12)—C(4)	-3
C(3)—C(4)—C(12)—N(10)	179	C(1)—C(11)—C(12)—N(10)	180
C(3)—C(4)—C(12)—C(11)	2	C(9)—C(11)—C(12)—C(4)	174
C(13)—C(5)—C(6)—C(7)	-1	C(9)—C(11)—C(12)—N(10)	-3
C(6)—C(5)—C(13)—N(10)	-179	C(5)—C(13)—C(14)—C(8)	4
C(6)—C(5)—C(13)—C(14)	-3	C(5)—C(13)—C(14)—C(9)	-176
C(5)—C(6)—C(7)—C(8)	3	N(10)—C(13)—C(14)—C(8)	180
C(6)—C(7)—C(8)—C(14)	-2	N(10)—C(13)—C(14)—C(9)	0
C(7)—C(8)—C(14)—C(9)	178	C(9)—N(18)—C(19)—C(20)	-163
C(7)—C(8)—C(14)—C(13)	-2	N(18)—C(19)—C(20)—C(21)	-70
C(14)—C(9)—C(11)—C(1)	-158	C(19)—C(20)—C(21)—N(22)	170
C(14)—C(9)—C(11)—C(12)	25	C(20)—C(21)—N(22)—C(23)	156
N(18)—C(9)—C(11)—C(1)	24	C(20)—C(21)—N(22)—C(24)	-81

All calculations were performed on an ICL 4/70 computer using the NRC system of crystallographic programs<sup>11)</sup> and on an ODRA-1204 apparatus using programs written by Professor K. Łukaszewicz<sup>12)</sup>.

## DISCUSSION

The positional parameters of all atoms were used to calculate the geometry of the molecule and the packing in the unit cell. The atoms of C-283.HI are numbered and presented in Fig. 2. The bond lengths and angles are listed in Tables 7 and 8, respectively. The torsional angles are given in Table 9. The packing of the molecules in the unit cell is illustrated in Figs 3 and 4.

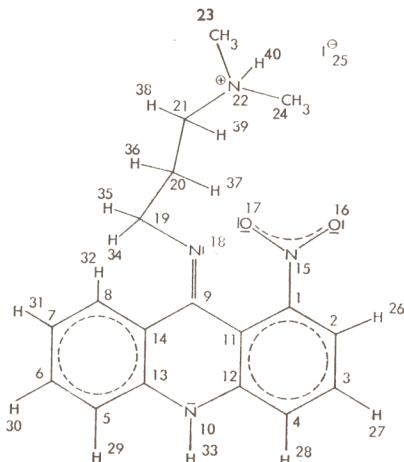


Fig. 2. Numbering of atoms

Rys. 2. Numeracja atomów

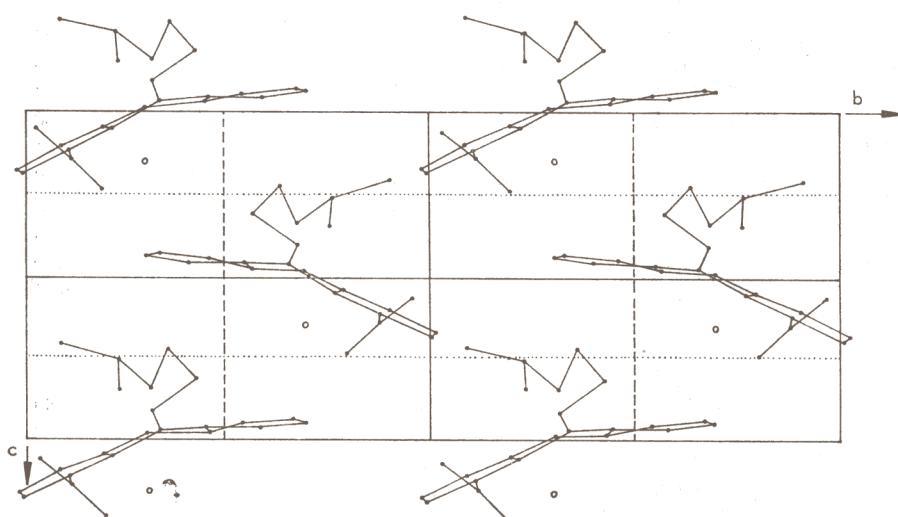


Fig. 3. Packing of molecules in the unit cell along the *a* axis  
Rys. 3. Upakowanie cząsteczek w komórce elementarnej wzdłuż osi *a*

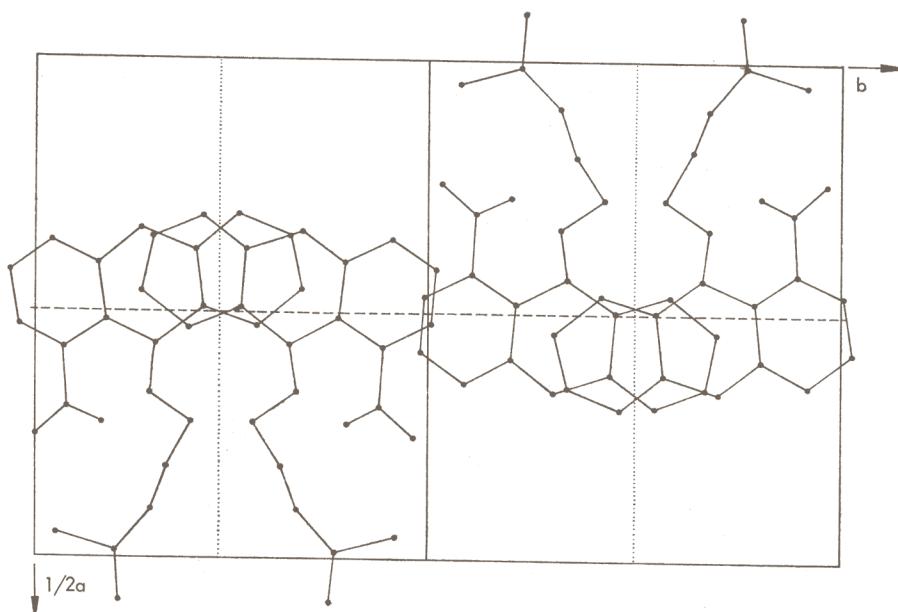


Fig. 4. Packing of molecules in the unit cell along the *c* axis  
Rys. 4. Upakowanie cząsteczek w komórce elementarnej wzdłuż osi *c*

The nearest molecules of the unit cell are stacked above and below each other at about 3.9 Å apart. They are related by a glide plane of the *c* type and arranged in head-to-head order, in contrast to other crystal structures of acridine derivatives which are for the most part arranged in head-to-tail mode. The shortest intermolecular contacts are presented in Table 10. Every two acridine cations are hydrogen bound with the iodide anion, as illustrated in Table 11.

The aliphatic side chain is unstrained and the atoms are linked forming either a synclinal or an anticalinal conformation. Only the dimethylamino N(22) group is distorted in relation to the methylene group at C(21), bringing about a conformation where the hydrogen atom H(40) is closer

Table 10 — Tablica 10  
Intermolecular distances shorter than 3.5 Å  
Kontakty międzymięczystekowe krótsze niż 3,5 Å

C(2) <sup>i</sup> —C(7) <sup>ii</sup>	3.493 Å
C(6) <sup>i</sup> —C(12) <sup>iii</sup>	3.379
C(7) <sup>i</sup> —C(11) <sup>iii</sup>	3.292
C(7) <sup>i</sup> —C(12) <sup>iii</sup>	3.316

Symmetry:

- i             $x, y, z$
- ii           $1/2-x, 1/2+y, z$
- iii         $x, 1/2-y, 1/2+z$

Table 11 — Tablica 11  
Hydrogen bonds — Wiązania wodorowe

N(10)<sup>i</sup>—N(33)...I(25)<sup>i</sup>      3.729 Å  
N(22)<sup>ii</sup>—H(40)...I(25)<sup>i</sup>      3.389

Symmetry:  
i         $x, y, z$   
ii       $1/2+z, y, 3/2-z$

Table 12 — Tablica 12  
Deviations (Å) of atoms from least-squares planes  
Odchylenia atomów od średnich płaszczyzn w Å

Atom	I	II	III	IV
C(1)	-0.119	-0.039		-0.0010
C(2)	-0.285	0.009		
C(3)	-0.248	-0.025		
C(4)	-0.031	0.018		
C(5)	-0.038		0.020	
C(6)	-0.252		0.030	
C(7)	-0.313		-0.019	
C(8)	-0.091		-0.020	
C(9)	0.436	0.053	0.034	
N(10)	0.377	-0.010	-0.018	
C(11)	0.128	-0.028		
C(12)	0.136	-0.028		
C(13)	0.137		-0.025	
C(14)	0.162		-0.020	
N(15)	-0.308*	-0.197*		0.0034
O(16)	0.506*	0.734*		-0.0013
O(17)	-1.249*	-1.227*		-0.0011
N(18)	0.946*	0.588*	0.499*	
Mean deviation	0.230	0.030	0.023	0.0014

Planes equations ( $X, Y, Z$  in Å):

$$\begin{array}{lll} \text{I} & (\text{A,B,C}) & 0.015 X-0.258 Y-0.966 Z = -8.523 \\ \text{II} & (\text{A}) & 0.039 X-0.427 Y-0.903 Z = -8.064 \\ \text{III} & (\text{C}) & -0.011 X-0.075 Y-0.997 Z = -7.921 \\ \text{IV} & (\text{NO}_2) & 0.065 X+0.635 Y-0.770 Z = -5.603 \end{array}$$

Angles between planes:

$$\begin{array}{ll} \text{I-II} & 10.44^\circ \\ \text{I-III} & 10.79 \\ \text{II-III} & 21.23 \\ \text{II-IV} & 64.75 \end{array}$$

\* Atoms not used to define the least-square planes.

Table 13 — Tablica 13  
 Averaged bond lengths of left and right sides of acridine nucleus in 9-aminoacridine derivatives  
 Uśrednione po obu połowach rdzenia akrydynowego długosci wiązań w pochodnych 9-aminoakrydynowych

	Ref.	C(1)—C(2)	C(2)—C(3)	C(3)—C(4)	C(4)—C(5)	C(5)—C(6)	C(6)—C(7)	C(7)—C(8)	C(8)—C(11)	C(11)—C(12)	C(12)—C(13)	C(13)—C(14)	C(14)—C(11)	C(11)—C(9)	C(9)—NHR	N(10)—C(12)	N(10)—C(13)	C—N(10)—C	Angle
9-NH <sub>2</sub> -Ac. HCl	17	1.362	1.406	1.360	1.417	1.411	1.410	1.436	1.360	1.321	1.19	1.23							
Atebrine. 2HCl	18	1.358	1.406	1.357	1.425	1.413	1.416	1.440	1.359	1.347	1.18	1.22							
Acrid.-anilide. HCl	19	1.360	1.410	1.351	1.418	1.403	1.424	1.432	1.360	1.353	1.19	1.23							
ICR-449-OH	20	1.361	1.405	1.353	1.424	1.425	1.421	1.434	1.357	1.345	1.17	1.16							
ICR-170-OH	21	1.360	1.407	1.360	1.428	1.430	1.429	1.423	1.347	1.363	1.18	1.17							
ICR-171-OH	22	1.366	1.398	1.364	1.428	1.428	1.424	1.430	1.354	1.336	1.17	1.17							
ICR-191-OH	23	1.365	1.396	1.343	1.418	1.423	1.421	1.431	1.353	1.342	1.17	1.17							
Mean value		1.362	1.404	1.355	1.423	1.419	1.421	1.432	1.356	1.344	1.18	1.17*							
C-283.HI	this work	1.390	1.362	1.382	1.413	1.375	1.436	1.464	1.391	1.313	1.15	1.22**							

\* Free bases.

\*\* N(10)-Protonized compounds.

to the iodide ion I(25), so that a hydrogen bond of N(22)—H(40)...I(25) type can be formed. Owing to the steric interaction of two methyl groups, the sum of valence angles at N(22) is  $333^\circ$ , slightly exceeding the value of  $327.5^\circ$  for  $sp^3$  hybridization. The acridine nuclei are not planar but folded by  $20^\circ$  around C(9)—N(10) direction in such a way that the molecule looks like a butterfly, its wings made of A and C side rings. The differences between the corresponding bond lengths of the A and C rings are not greater than the sum of their standard deviations and are within the range of 0.02—0.03 Å. Only the C(2)—C(3) bond length is by about 0.05 Å longer than that of C(6)—C(7). The nitro group atoms and the carbon atom C(1) lie in the plane which intersects the one containing the A ring atoms at an angle of  $64^\circ$ . The least-square planes through various groups of atoms are shown in Table 12.

The sum of the valence angles at C(9) is  $360^\circ$  and agrees with the theoretical value for  $sp^2$  hybridization. The group of C(9), C(11), C(14) and N(18) atoms is planar. Due to steric interaction between the C(19) methylene group and the H(32) hydrogen atom, and to the short C(8)—C(19) distance of 3.06 Å, the N(18)—C(9)—C(14) and C(9)—N(18)—C(19) angles are larger than the theoretical value of  $120^\circ$ , being  $129$  and  $124^\circ$ , respectively. The  $122^\circ$  angle at C(11)—N(10)—C(13) is characteristic of acridinium form, but not of the free acridine base<sup>13)</sup>. A comparison made between the bond lengths of C-283.HI and other aminoacridine derivatives reveals substantial differences in the structure of these compounds. The bond lengths in the central acridine B ring are considerably lengthened in C-283.HI compared to those of other aminoacridine derivatives (cf. Table 13). The C(9)—N(18) bond length being 1.313 Å is shorter than that in other 9-aminoacridines (1.34—1.36 Å) and also for 9-aminoacridine hydrochloride (1.32) and for atebrine dihydrochloride (1.35 Å) (cf. Table 13).

The changes observed in C-283.HI bond length result from the fact that the conjugated ring system adopts different electronic structure. The aromatic character of the central B ring is decreased owing to non-planarity of the molecule. The occurrence of the C-283 in an imino-tautomeric form is confirmed by the position of H(33) at N(10) and by the bond lengths of the acridine nucleus. Non-coplanarity of the A and C side rings and the distortion of the nitro group is attributable to non-bonded contacts of the  $-NO_2$  and  $=NR$  substituents. Thus, there are two unconjugated benzene-type rings, A and C, in the molecule. The  $\pi$ -electrons of the N(10), C(9) and N(18) atoms tend to locate at the N(10) atom and along the C(9)—N(18) bond. In this connection, the mesomeric form with double imino-bond and a free electron pair at N(10) contribute essentially to the electronic structure of the molecule. It results therefrom that C-283.HI. has an iminoacridine tautomeric form with the H(33) hydrogen atom at N(10), since it is only then that there is no need for the charge to be separated. The twist of the nitro group by about  $60^\circ$  from the A ring plane prevents this group from conjugating with the rest of the molecule. It is not because of the induction effects brought about by formation of intramolecular hydrogen bonds that the nitro group in the C-283 easily undergoes reduction reactions<sup>14)</sup>, but because of electronic deficiency caused by the lack of mesomeric effect.

NMR spectroscopic studies<sup>15)</sup> and kinetic investigations on hydrolysis of C-283 and its various analogs also prove the compounds to be mainly imino forms in aqueous solutions<sup>16)</sup>. Such a geometry of the molecule and

its electronic structure stabilize the iminoacridane form even in solution. Hence, the stereochemistry of the molecule in solution is closely related to that of the crystal structure.

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**BADANIA RENTGENOGRAFICZNE POCHODNYCH AKRYDYNY.  
I. STRUKTURA KRYSТАLICZNA I MOLEKULARNA  
MONOJODOWODORKU  
1-NITRO-9(3-DIMETYLOAMINOPROPYLOAMINO)-AKRYDYNY**

**Z. DAUTER, M. BOGUCKA-LEDÓCHOWSKA, A. HEMPEL,  
A. LEDÓCHOWSKI i Z. KOSTURKIEWICZ**

*Zakład Technologii Leków i Biochemii Politechniki, 80952 Gdańsk  
Zakład Krystalografii Uniwersytetu A. Mickiewicza, 60780 Poznań*

Określono strukturę krystaliczną i molekularną 1-nitro-9(3-dimetyloaminopropylamino)-akrydyny w postaci monojodowodorku metodą rentgenowskiej analizy strukturalnej. Związek ten w postaci dwuchlorowodorku wprowadzony został do lecznictwa pod nazwą Ledakrin.

Strukturę rozwiązyano metodą Pattersona oraz kolejnych przybliżeń gęstości elektronowej, a następnie udokładniono metodą najmniejszych kwadratów blokowo-diagonalnie oraz pełnomacierzowo, uzyskując wskaźnik rozbieżności  $R = 6,3\%$ .

Stwierdzono, że rdzeń akrydynowy jest zgięty wzduż linii C(9)—N(10) o  $20^\circ$ . Grupa nitrowa jest skręcona względem płaszczyzny sąsiedniego pierścienia benzenowego o ponad  $60^\circ$ . Wiązanie C(9)—N(18) ma częściowo podwójny charakter ( $1,312 \text{ \AA}$ ), zaś wiązania w środkowym pierścieniu akrydyny są wydłużone. Na podstawie różnicowej mapy Fouriera stwierdzono obecność atomu wodoru przy pierścieniowym atomie azotu N(10). Badany związek występuje więc w iminoakrydanowej formie tautomerycznej.